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(57) Abstract: The present invention provides methods and compositions for treating bacterial infections, especially infections by opportunistic pathogens in a subject by administering a compound that inhibits syndecan-1 shedding. The invention is based on the discovery that two diverse opportunistic pathogens, S. aureus and P. aeruginosa, enhance syndecan-1 shedding and that this shedding is critical for Pseudomonas pathogenesis via the respitory tract. The discovery is also based on the surprising finding that inhibition of syndecan-1 shedding prevents Pseudomonas pneumonia in a mammalian model. The P. aeruginosa shedding enhancer has been purified and identified as the mature 20 kDa LasA protein, a known virulence factor of P. aeruginosa.